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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/543,048	01/26/2006	Philipp Hadwiger	26421-15811 US	3878
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ALNYLAM/FENWICK SILICON VALLEY CENTER 801 CALIFORNIA STREET MOUNTAIN VIEW, CA 94041				
EXAMINER				
CHONG, KIMBERLY				
ART UNIT		PAPER NUMBER		
1635				
NOTIFICATION DATE		DELIVERY MODE		
03/11/2010		ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Advisory Action
Before the Filing of an Appeal Brief

Application No.

10/543,048

Applicant(s)

HADWIGER ET AL.

Examiner

KIMBERLY CHONG

Art Unit

1635

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12 February 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
The status of the claim(s) is (or will be) as follows:
Claim(s) allowed: _____.
Claim(s) objected to: _____.
Claim(s) rejected: _____.
Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____.
13. ☐ Other: _____.

/Kimberly Chong/
Primary Examiner AU1635

Continuation of 11, does NOT place the application in condition for allowance because: Applicant's arguments do not overcome the rejections of record. Applicant continues to argue that Rana continues to teach the importance and necessity of the 5' end hydroxyl of the antisense strand of an siRNA for RNAi activity. First it must be pointed out that Rana has not been used as a prior art reference in the 103 rejection of record. Applicant appears to use Rana as evidence that the prior art teach that the 5' end of the antisense strand should contain a free OH group. The prior art demonstrates that as long as the 5' end of the antisense strand contains a phosphate group, the dsRNA appears to remain amenable to RNAi as demonstrated by Schwarz et al. who teach a dsRNA wherein the 5' end was linked with a phosphodiester linkage. Applicant did not address the Schwarz et al. reference as evidence of what was taught in the prior art. Thus because Rana was not used in the rejection of record as motivation to not modify the 5' end of an antisense strand of a dsRNA and because it was known in the prior art that a dsRNA containing a phosphodiester group at the 5 end was amenable to RNAi, this argument is not persuasive. Applicant argues Fosnaugh et al. teach too many variations and one would not arrive at the claimed invention with a reasonable expectation of success. As stated previously, given there are a finite number of identified predictable solutions for attaching a lipophilic group to either of 4 positions of a dsRNA, a skilled artisan would have a good reason to modify said dsRNA with a reasonable expectation of success. The claimed dsRNA broadly recites attached any lipophilic group to the 5' end wherein the 5' end comprises a phosphodiester group and does not recite any unexpected results that would make the claimed invention non-obvious to the skilled artisan. Lastly Applicant argues Florence does not teach the claimed logKow value because both describe the log of the partition coefficient and that these terms are the same and therefore Florence teach the log as 1.24 which is not the claimed log of greater than 1.5. This is not persuasive because Florence was cited for teach a conjugate with a partition coefficient of a certain value and as explained in the instant specification, the lipophilic group is defined by the partition coefficient. There is nothing in either the specification or Florence that defines the log P and logKow as equivalent. Thus the rejections of record are maintained.